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Parallelism between central and enteric nervous system damage in experimental parkinsonism

Antuela Matarangasi[1], Larisa Ryskalin[1], Chiara Pizzanelli[2], Antonio Pellegrini[1], Gianfranco Natale[1] and Antonio Paparelli[1]

[1] Department of Human Morphology and Applied Biology, University of Pisa, Pisa, Italy
[2] Department of Neuroscience, Neurological Clinic, University of Pisa, Pisa, Italy

Parkinson's disease (PD) is a neurodegenerative condition which affects dopaminergic neurons of the substantia nigra (SN), leading to a movement disorder. Non motor alterations occur in several viscera, in particular the gastrointestinal tract. In 9-week old C57BL mice we examined the effects of the parkinsonism-inducing neurotoxin 1-methyl, 4-phenyl, 1,2,3,6,-tetrahydropyridine (MPTP, administered either acutely or chronically) in SN and striatum, as well as in duodenum. Motor tests (open field and PaGE) were performed. One week after treatment with MPTP (acute: 20 mg/KgX3, 2h apart or chonic: 5 mg/kg x2/die, for 3 weeks), histological investigations, immunohistochemistry and immunoblotting for tyrosine hydroxylase (TH), and α-synuclein (α-syn) were carried out. Immunocytochemical investigations were analyzed under electron microscopy. Motor tests showed a failure of the PaGE test in all MPTP-treated animals, whereas no difference was found in open field test in comparison with controls. Analysis of histological sections showed some alterations consisting of slight atrophy of duodenal mucosa and glandular disarrangement only after chronic treatment. Under electron microscopy the brush border appeared discontinuous. In all MPTP-administered mice, TH immunopositivity was reduced in SN and striatum, confirming its central dopaminergic neurotoxicity. At duodenal level, TH immunostaining was lost following all MPTP treatments with a slight variation in chronic compared with acute administrations. This was confirmed by semiquantitative immunoblotting. Moreover, α-syn immunostaining was enhanced by MPTP treatment but this was way more evident following chronic administration both at central and peripheral level. Following chronic treatment α-Syn immunopositive structures were investigated under electron microscopy. Our study shows that chronic more than acute administration of MPTP induces alterations at duodenal level reminiscent of dopaminergic damage in SN and striatum. Moreover, this experimental model of parkinsonism features gastrointestinal dysfunction observed in PD patients. These findings lend substance to the concept of the enteric nervous system as a double brain which recapitulates and is an ancestry of the central nervous system.

Keywords: Duodenum, mouse, Parkinson's disease, α-synuclein, tyrosine hydroxylase.